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E9 5 SPEAR MICHAEL/AU
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L1 44 ("SPEAR MATT A"/AU OR "SPEAR MATTHE?"/AU OR "SPEAR MATTHEW"/AU
OR "SPEAR MATTHEW A"/AU OR "SPEAR MATTHEW ADRIAN"/AU)

=> dupr rem 11
MISSING OPERATOR REM L1
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L2 28 DUP REM L1 (16 DUPLICATES REMOVED)

=> cells and 12
L3 12 CELLS AND L2

=> library and 12
L4 4 LIBRARY AND L2

=> ligand and 12
L5 3 LIGAND AND L2

=> apoptosis and 12
L6 1 APOPTOSIS AND L2

=> t ti 12 1-28

L2 ANSWER 1 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI A Phase 1 accelerated titration dose escalation study of the vascular disrupting agent NPI-2358 utilizing DCE-MRI.

L2 ANSWER 2 OF 28 MEDLINE on STN DUPLICATE 1
TI Phase I/II study of IV topotecan in combination with whole brain radiation for the treatment of brain metastases.

L2 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
TI Use of MEK inhibitors in treating abnormal cell growth

L2 ANSWER 4 OF 28 MEDLINE on STN DUPLICATE 2
TI Focal radiation therapy of brain metastases after complete surgical resection.

L2 ANSWER 5 OF 28 MEDLINE on STN
TI Temozolomide and radiation for aggressive pediatric central nervous system malignancies.

L2 ANSWER 6 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Herpes simplex virus amplicon vector targeting system and method of using same.

L2 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 3
TI HSV-1 virions engineered for specific binding to cell surface receptors.

L2 ANSWER 8 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI alpha 5 beta 1 integrin targeted HSV-1 amplicon vector.

L2 ANSWER 9 OF 28 MEDLINE on STN DUPLICATE 4
TI Targeting HSV amplicon vectors.

L2 ANSWER 10 OF 28 MEDLINE on STN DUPLICATE 5
TI HSV-1 amplicon peptide display vector.

L2 ANSWER 11 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Peptide display library in an HSV-1 amplicon vector system selected against prostate carcinoma cells.

L2 ANSWER 12 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Molecular glial progression: Mutant, wild type or overall p53 expression?.

L2 ANSWER 13 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
TI Isolation, characterization, and recovery of small peptide phage display epitopes selected against viable malignant glioma cells.

L2 ANSWER 14 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Oncolytic herpes simplex virus type-1 vector with anti-K-ras antisense oligonucleotides.

L2 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
TI Herpes simplex virus amplicon vector targeting system and method of using same

L2 ANSWER 16 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
TI Cytotoxicity, apoptosis, and viral replication in tumor cells treated with oncolytic ribonucleotide reductase-defective herpes simplex type 1 virus (hrR3) combined with ionizing radiation.

L2 ANSWER 17 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Efficient DNA subcloning through selective restriction endonuclease digestion.

L2 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
TI Efficient DNA subcloning through selective restriction endonuclease digestion

L2 ANSWER 19 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Phage display epitopes selected against viable glioblastoma cells for insertion into an HSV-1 amplicon vector targeting system.

L2 ANSWER 20 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 8
TI Improved method for transport of living cell cultures.

L2 ANSWER 21 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Mechanisms of radiation sensitization by recombinant methioninase (rMETase).

L2 ANSWER 22 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Tolerance of autologous and allogeneic bone grafts to therapeutic radiation in humans.

L2 ANSWER 23 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 9
TI Gene therapy of gliomas: Receptor and transcriptional targeting.

L2 ANSWER 24 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 10
TI Mapping the in vivo distribution of herpes simplex virions.

L2 ANSWER 25 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Individualizing management of aggressive fibromatoses.

L2 ANSWER 26 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 11
TI Targeting gene therapy vectors to CNS malignancies.

L2 ANSWER 27 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Benign and low-grade tumors of the soft tissues: Role for radiation therapy.

L2 ANSWER 28 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 12
TI Toxicology of daily administration to mice of the radiation potentiator SR-4233 (WIN-59075).

=> d ibib abs 12 1-28

L2 ANSWER 1 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:301596 BIOSIS
DOCUMENT NUMBER: PREV200700306724
TITLE: A Phase 1 accelerated titration dose escalation study of
the vascular disrupting agent NPI-2358 utilizing DCE-MRI.
AUTHOR(S): Lorusso, Patricia [Reprint Author]; Papadopoulos, Kyri;
Tolcher, Anthony; Lin, Chia-Chi; Lloyd, Kenneth; Morgan,
Elizabeth; Ashton, Edward; Cropp, Gillian; Spear,
Matthew A.
CORPORATE SOURCE: Karmanos Canc Ctr, Detroit, MI USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (APR 2007) Vol. 48, pp. 943.
Meeting Info.: 98th Annual Meeting of the
American-Association-for-Cancer-Research. Los Angeles, CA,
USA. April 14 -18, 2007. Amer Assoc Canc Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 May 2007
Last Updated on STN: 9 May 2007

L2 ANSWER 2 OF 28 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2007535731 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17848737
TITLE: Phase I/II study of IV topotecan in combination with whole
brain radiation for the treatment of brain metastases.
AUTHOR: Mirmiran Alireza; McClay Edward; Spear Matthew A
.CORPORATE SOURCE: Radiation Oncology, UCSD Cancer Center, UCSD Medical
Center, 200 W Arbor Dr, San Diego, CA, 92103.
SOURCE: Medical oncology (Northwood, London, England), (2007) Vol.
24, No. 2, pp. 147-53.
Journal code: 9435512. ISSN: 1357-0560.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED;
Priority Journals
ENTRY DATE: Entered STN: 14 Sep 2007
Last Updated on STN: 14 Sep 2007

AB A phase I/II trial was conducted to determine the toxicities and efficacy
(overall response, overall survival, and progression-free survival) of the
combination of topotecan and whole brain radiation therapy (XRT) in
patients with brain metastases. Patients received 30 Gy XRT given in 10
fractions to the whole brain. In phase I, patients were treated in groups
of three at each topotecan dose level; dose escalation proceeded until the
maximum tolerated dose (MTD) was identified. The dose-limiting toxicity
proved to be grade IV neutropenia at 0.6 mg/m²/d, resulting in an MTD of
0.5 mg/m²/d. One of nine patients showed a response to treatment, and
that was partial (OR 11%). Three had stable disease (33%), and four
experienced progressive disease (44%). Median progression-free survival
was 60 d; median overall survival was 102 d. Intravenous topotecan at 0.5
mg/m²/d concomitant to XRT with 30 Gy in 3-Gy fractions is tolerable in
patients with brain metastases. This regimen has the additional advantage
of providing systemic treatment to patients with metastases in other
locations while whole brain radiation is in progress. Although response
and survival outcomes in this small study do not appear higher than
expected from historical controls, these were not primary end points, and
larger studies on this topic would be useful to elucidate the efficacy of

this combination treatment regimen.

L2 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:578085 CAPLUS
DOCUMENT NUMBER: 145:55919
TITLE: Use of MEK inhibitors in treating abnormal cell growth
INVENTOR(S): Deprimo, Samuel Eugene; Leopold, Judith Ann; Meyer,
Mark Bradley; Sadis, Seth Edward; Spear, Matthew
Adrian; Tan, Weiwei; Whitfield, Lloyd Richard
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2006061712 | A2 | 20060615 | WO 2005-IB3737 | 20051129 |
| WO 2006061712 | A3 | 20060727 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |
| US 2006154990 | A1 | 20060713 | US 2005-298084 | 20051208 |
| PRIORITY APPLN. INFO.: US 2004-635149P P 20041210
US 2005-648972P P 20050131
US 2005-680854P P 20050512
US 2005-708311P P 20050815 | | | | |

AB The invention provides the use of N-[(R)-2,3-dihydroxy-propoxy]-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)benzamide for treating abnormal cell growth in mammals. In particular, the invention provides dosage regimes for administration of N-[(R)-2,3-dihydroxy-propoxy]-3,4-difluoro-2-(2-fluoro-4-iodo-phenylamino)benzamide to mammals suffering from cancer.

L2 ANSWER 4 OF 28 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006589166 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 17018888
TITLE: Focal radiation therapy of brain metastases after complete surgical resection.
AUTHOR: Bahl Gautam; White Greg; Alksne John; Vemuri Lakshmi;
Spear Matthew A
CORPORATE SOURCE: Radiation Oncology, Surgery and Hematology/Oncology, Moores UCSD Cancer Center, University of California at San Diego, San Diego, CA 92121.
SOURCE: Medical oncology (Northwood, London, England), (2006) Vol. 23, No. 3, pp. 317-24.
Journal code: 9435512. ISSN: 1357-0560.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED;
Priority Journals
ENTRY DATE: Entered STN: 5 Oct 2006

Last Updated on STN: 12 Dec 2006

AB Brain metastases are a frequent occurrence in cancer patients and result in significant morbidity and mortality. The three main treatments for brain metastases include surgery, radiation, and/or chemotherapy, alone or in combination. After resection alone, local recurrence rates are high. Whole brain radiation therapy can decrease the probability of recurrence; however, this has some disadvantages. Focal radiation therapy (FRT) may provide many of the same benefits without some of these disadvantages. In this study, we retrospectively analyzed patients with single brain metastases treated with FRT after surgery. Doses ranged from 14 Gy as single dose stereotactic radiosurgery (SRS) to 54 Gy in 27 2-Gy fractions as conformal fractionated radiotherapy. Four of the seven patients had a same-site recurrence, with an average time to recurrence of 115.5 d. Median dose in the patients that had same-site recurrence was 42 Gy. One of these patients is currently living. Two patients did not have recurrence, and one patient had a recurrence at a different site within the brain. The low rate of out-of-field recurrences during the patients life indicates focal radiation may be a reasonable therapeutic alternative. Given the number of patients with same-site recurrences, wide field margins around the tumor volume or higher radiation doses than those typically used in palliative regimens may be useful in postexcisional FRT. Additionally, we found that a longer delay in the initiation of FRT after initial diagnosis may result in a decreased time to same-site recurrence. However, further studies are warranted given the small number of patients in this study.

L2 ANSWER 5 OF 28 MEDLINE on STN
ACCESSION NUMBER: 2005281727 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15891559
TITLE: Temozolomide and radiation for aggressive pediatric central nervous system malignancies.
AUTHOR: Loh Kenneth C; Willert Jennifer; Meltzer Hal; Roberts William; Kerlin Bryce; Kadota Richard; Levy Michael; White Greg; Geddis Amy; Schiff Deborah; Martin Laura; Yu Alice; Kung Faith; Spear Matthew A
CORPORATE SOURCE: Department of Radiation Oncology, UCSD Cancer Center, University of California at San Diego, San Diego, California 92103, USA.
SOURCE: Journal of pediatric hematology/oncology : official journal of the American Society of Pediatric Hematology/Oncology, (2005 May) Vol. 27, No. 5, pp. 254-8.
Journal code: 9505928. ISSN: 1077-4114.

PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 2 Jun 2005
Last Updated on STN: 6 Jul 2005
Entered Medline: 5 Jul 2005

AB This study describes the outcomes of children treated with combinations of temozolomide and radiation therapy for various aggressive central nervous system malignancies. Their age at diagnosis ranged from 1 to 15 years. Patients with focal disease were treated with concomitant temozolomide (daily 75 mg/m²) and three-dimensional conformal radiotherapy in a dose that ranged from 50 to 54 Gy, followed by temozolomide (200 mg/m²/d x 5 days/month in three patients, 150 mg/m² x 5 days/month in one patient). Patients with disseminated disease were treated with craniospinal radiation (39.6 Gy) before conformal boost. One patient received temozolomide (200 mg/m² x 5 days/month) before craniospinal radiation, and one patient received temozolomide (daily 95 mg/m²) concomitant with craniospinal radiation and a radiosurgical boost, followed by temozolomide

(200 mg/m² x 5 days/month). Three patients achieved a partial response during treatment, with two of these patients dying of progressive disease after treatment. One patient has no evidence of disease. Three patients achieved stable disease, with one of these patients dying of progressive disease after treatment. Toxicities observed included low-grade neutropenia, thrombocytopenia, and lymphopenia. The combination of temozolamide and radiotherapy appears to be well tolerated in a variety of treatment schemas for aggressive pediatric central nervous system malignancies. This information is of particular use in designing future studies, given the recent positive results in a randomized study examining the use of temozolamide concomitant with radiation in the treatment of adult glioblastoma.

L2 ANSWER 6 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:90123 BIOSIS
DOCUMENT NUMBER: PREV200400094659
TITLE: Herpes simplex virus amplicon vector targeting system and method of using same.
AUTHOR(S): Spear, Matthew A. [Inventor, Reprint Author]; Breakefield, Xandra O. [Inventor]
CORPORATE SOURCE: San Diego, CA, USA
ASSIGNEE: The General Hospital Corporation; The Regents of the University of California
PATENT INFORMATION: US 6673602 20040106
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan 6 2004) Vol. 1278, No. 1.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Feb 2004
Last Updated on STN: 11 Feb 2004
AB The present invention relates to herpes simplex virus (HSV) amplicon vectors, and in particular, HSV-1 amplicon vectors, which have been genetically modified and used alone or with consequent genetically modified HSV virus, to target a selected cell type, such as neoplastic cells. The present invention also relates to methods of using such vectors to target a cell, in order to treat a pathologic condition, such as cancer.

L2 ANSWER 7 OF 28 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004117265 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15006609
TITLE: HSV-1 virions engineered for specific binding to cell surface receptors.
AUTHOR: Grandi Paola; Wang Samuel; Schuback Deborah; Krasnykh Victor; Spear Matthew; Curiel David T; Manservigi Roberto; Breakefield Xandra O
CORPORATE SOURCE: Department of Neurology and Department of Radiology, Massachusetts General Hospital, and Neuroscience Program, Harvard Medical School, Boston, MA 02129, USA.
CONTRACT NUMBER: NS28384 (NINDS)
NS37409 (NINDS)
P50 CA89019 (NCI)
R01CA86881 (NCI)
SOURCE: Molecular therapy : the journal of the American Society of Gene Therapy, (2004 Mar) Vol. 9, No. 3, pp. 419-27.
Journal code: 100890581. ISSN: 1525-0016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 9 Oct 2004
Entered Medline: 8 Oct 2004

AB Expression of specific peptide epitopes on the surface of virions has significant potential for studying viral biology and designing vectors for targeted gene therapy. In this study, an HSV-1 amplicon plasmid expressing a modified glycoprotein C (gC), in which the heparan sulfate binding domain was replaced with a His-tag, was used in generating HSV-1 virions. Western blot analysis demonstrated the presence of modified gC in the purified virions. The amplicon vectors were packaged using a gC-, lacZ+ helper virus to generate a mixture of high-titer helper virus (lacZ+) and amplicon vectors (GFP+), which expressed modified gC in the virion envelope. His-tagged virions bound to 293 6H cells expressing a cell surface pseudo-His-tag receptor four-fold more efficiently than to parental 293 cells and also proved more effective than wild-type virus in binding to both cell types. Binding resulted in productive infection by the modified virions with expression of reporter genes and cytopathic effect comparable to those of wild-type virions. Thus, not only can HSV-1 tropism be manipulated to recognize a non-herpes simplex binding receptor, but it is also possible to increase the infective capacity of the vectors beyond that of the wild-type virus via specific ligand receptor combinations.

L2 ANSWER 8 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:253526 BIOSIS
DOCUMENT NUMBER: PREV200700275518
TITLE: alpha 5 beta 1 integrin targeted HSV-1 amplicon vector.
AUTHOR(S): Spear, Matthew A. [Reprint Author]; Elsaesser,
Heidi; Yoo, Linda; Varner, Judy
CORPORATE SOURCE: Univ Calif San Diego, Ctr Canc, San Diego, CA 92103 USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (MAR 2004) Vol. 45, pp. 270.
Meeting Info.: 95th Annual Meeting of the
American-Association-for-Cancer-Research. Orlando, FL, USA.
March 27 -31, 2004. Amer Assoc Canc Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2007
Last Updated on STN: 11 Jul 2007

L2 ANSWER 9 OF 28 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004223458 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15121173
TITLE: Targeting HSV amplicon vectors.
AUTHOR: Grandi Paola; Spear Matthew; Breakefield Xandra
O; Wang Samuel
CORPORATE SOURCE: Departments of Neurology and Radiology, Massachusetts
General Hospital and Neuroscience Program, Harvard Medical
School, Charlestown, MA 02129, USA.
CONTRACT NUMBER: CA69246 (NCI)
CA86355 (NCI)
SOURCE: Methods (San Diego, Calif.), (2004 Jun) Vol. 33, No. 2, pp.
179-86.
Journal code: 9426302. ISSN: 1046-2023.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 5 May 2004
Last Updated on STN: 22 Dec 2004
Entered Medline: 21 Dec 2004

AB Several techniques have been developed to deliver DNA directly into mammalian cells, spanning in difficulty from simple mixing procedures to complex systems requiring expensive equipment. Viral vectors have proven able to deliver genes into mammalian cells with high efficiency and low toxicity. In particular, herpes simplex virus type-1 (HSV-1) amplicon vectors are well suited for gene transfer studies as they can infect many cell types, both non-dividing and dividing, have a large transgene capacity and are easy to manipulate. For some applications, it may be desirable to target gene delivery to specific cell populations or to transduce normally non-susceptible cells. This can be achieved by modifying one or more of the glycoproteins found in the viral envelope. Glycoprotein C (gC) has a well-characterized heparan sulfate binding domain (HSBD) necessary for HSV binding to cells. Replacing this region with unique ligands can result in less efficient binding to natural target cells and increase binding to cells which express receptors for these ligands. A method to retarget amplicon vectors by replacing gC HSBD with a model ligand, the hexameric histidine-tag, is described, as well as means to evaluate the binding of modified vector as compared to wild-type virus to cells with or without the appropriate receptor, in this case, a his-tag pseudo-receptor. This protocol demonstrates increased binding of modified virus to receptor-positive cells (at levels greater than wild-type) with no loss of infectivity. Retargeted vectors can provide an additional tool for increasing the efficiency of gene delivery to specific cell types.

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L2 ANSWER 10 OF 28 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002688718 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12445940
TITLE: HSV-1 amplicon peptide display vector.
AUTHOR: Spear Matthew A; Schuback Deborah; Miyata Kenichi; Grandi Paola; Sun Fang; Yoo Linda; Nguyen Anh; Brandt Curtis R; Breakefield Xandra O
CORPORATE SOURCE: Gene Therapy Program, Radiation Oncology, UCSD Cancer Center, UCSD Medical Center, University of California San Diego, MC 8757, 200 West Arbor Drive, La Jolla, CA, USA.. mspear@ucsd.edu
CONTRACT NUMBER: CA 69246 (NCI)
SOURCE: Journal of virological methods, (2003 Jan) Vol. 107, No. 1, pp. 71-9.
Journal code: 8005839. ISSN: 0166-0934.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 14 Dec 2002
Last Updated on STN: 21 Feb 2003
Entered Medline: 20 Feb 2003

AB There are significant uses for expressing foreign peptide epitopes in viral surface attachment proteins in terms of investigating viral targeting, biology, and immunology. HSV-1 attachment, followed by fusion and entry, is mediated in large part by the binding of viral surface glycoproteins to cell surface receptors, primarily through heparan sulfate (HS) glycosaminoglycan residues. We constructed a HSV-1 amplicon plasmid (pCONGA) carrying the gC primary attachment protein gene with unique restriction sites flanking the HS binding domain (HSBD) (residues 33-176)

to allow rapid, high efficiency substitution with foreign peptide domains. To test this system, a His tag with an additional unique restriction site (for selection and assay digests) was recombined into the pCONGA HSBD site to create pCONGAH. Infection of pCONGAH transfected Vero cells with HSV-1 helper virus (gCdelta2-3 or hrR3) produced His-modified gC as demonstrated by western blot analysis with co-localization of anti-gC and anti-His tag antibodies to a protein of appropriate molecular weight (50 kd). As CONGA and CONGAH amplicons carry a GFP transgene and the gCdelta2-3 and hrR3 viruses carry a lacZ transgene, vector stocks produced from 1 x 10(5) Vero cells could be titered for competent vector on cell monolayers and were demonstrated to contain 2 x 10(5) amplicon vector transducing units (t.u.)/ml and 1 x 10(7) virus t.u./ml. As the amplicon plasmids also contain the neomycin resistance gene (neo(r)), long term vector producer cell lines were created using G418 selection. This amplicon system provides means to rapidly and efficiently generate HSV-1 amplicon and viral vector expressing surface attachment proteins modified with different peptide epitopes for investigational and therapeutic uses, with the advantages of an amplicon plasmid that can be used with interchangeable helper virus vectors, is designed specifically for easy manipulation, and carries GFP and neo(r) transgenes for marker and selection functions.

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L2 ANSWER 11 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:409331 BIOSIS
DOCUMENT NUMBER: PREV200200409331
TITLE: Peptide display library in an HSV-1 amplicon vector system selected against prostate carcinoma cells.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Miyata, Kenichi [Reprint author]
CORPORATE SOURCE: UCSD Cancer Center, San Diego, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 803. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jul 2002
Last Updated on STN: 31 Jul 2002

L2 ANSWER 12 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:512838 BIOSIS
DOCUMENT NUMBER: PREV200100512838
TITLE: Molecular glial progression: Mutant, wild type or overall p53 expression?
AUTHOR(S): Pardo, Francisco S. [Reprint author]; Su, Mei; Efird, James T.; Spear, Matthew A.; Fox, Howard S.; Malkin, David
CORPORATE SOURCE: Harvard Medical School, Boston, MA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 650. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002

L2 ANSWER 13 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 6

ACCESSION NUMBER: 2002:479821 BIOSIS
DOCUMENT NUMBER: PREV200200479821
TITLE: Isolation, characterization, and recovery of small peptide phage display epitopes selected against viable malignant glioma cells.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Breakefield, Xandra O.; Beltzer, James; Schuback, Deborah; Weissleder, Ralph; Pardo, Francisco S.; Ladner, Robert
CORPORATE SOURCE: Radiation Oncology, UCSD Medical Center, 200 West Arbor Drive, MC 8757, San Diego, CA, 92103, USA
mspear@ucsd.edu
SOURCE: Cancer Gene Therapy, (July, 2001) Vol. 8, No. 7, pp. 506-511. print.
ISSN: 0929-1903.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Sep 2002
Last Updated on STN: 11 Sep 2002

AB Phage display techniques rely on nearly random oligonucleotide sequences inserted into the protein III filament binding protein of an Escherichia coli filamentous phage M13 to generate a library of phage that express more than 10⁷ different peptides. Phage that expresses a sequence having high affinity for a specific molecule, cell, or tissue can then be isolated through selective binding and recovery. Selected phage cannot only be used as gene transfer vectors in themselves, but the small peptide epitopes can be sequenced and potentially recombined into the attachment proteins of viral vectors, or used by themselves to target other therapeutic agents and diagnostic imaging radiolabels. Most phage display selections are carried out against purified and/or fixed protein targets, raising concerns as to the relevance of the selected epitopes. We have selected phage from the CMTI library against viable U87-MG human malignant glioma cells using a derivation of biopanning. The library, which initially contained phage expressing 2X10⁷ different epitope sequences, collapsed after four rounds of selection such that 42% of recovered clones expressed a consensus sequence. Selective binding to viable adherent U87-MG cells was subsequently demonstrated under physiologic conditions at 167% (+27%) unselected phage using a novel, viable enzyme-linked immunosorbent assay technique. In comparison, there was no difference in binding to control 9L rat gliosarcoma, Panc-1 human pancreatic adenocarcinoma, T98-MG human malignant glioma, or AST-4 human malignant glioma cells of selected compared to unselected phage. Using polymerase chain reaction, the epitope was recovered with flanking unique restriction sites for recombination into a herpes simplex virus type-1 vector. This study demonstrates and discusses optimized methodologies for using phage display to target viable cells.

L2 ANSWER 14 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 2001:354283 BIOSIS
DOCUMENT NUMBER: PREV200100354283
TITLE: Oncolytic herpes simplex virus type-1 vector with anti-K-ras antisense oligonucleotides.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Hsu, Hui; Miyata, Kenichi; Chiang, Ming-Yi; Monia, Brett P.
CORPORATE SOURCE: Isis Pharmaceuticals, Carlsbad, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 31. print.
Meeting Info.: 92nd Annual Meeting of the American

Association for Cancer Research. New Orleans, LA, USA.
March 24-28, 2001. American Association for Cancer
Research.

ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Aug 2001
Last Updated on STN: 19 Feb 2002

L2 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:900771 CAPLUS
DOCUMENT NUMBER: 134:46757
TITLE: Herpes simplex virus amplicon vector targeting system
and method of using same
INVENTOR(S): Spear, Matthew A.; Breakefield, Xandra O.
PATENT ASSIGNEE(S): The General Hospital Corp., USA; The Regents of the
University of California
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2000077167 | A2 | 20001221 | WO 2000-US16050 | 20000612 |
| WO 2000077167 | A3 | 20040506 | | |
| W: CA, JP | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE | | | | |
| US 6673602 | B1 | 20040106 | US 2000-592537 | 20000612 |
| EP 1444353 | A2 | 20040811 | EP 2000-938260 | 20000612 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI, CY | | | | |
| PRIORITY APPLN. INFO.: | | | US 1999-138963P | P 19990611 |
| | | | WO 2000-US16050 | W 20000612 |

AB The present invention relates to herpes simplex virus (HSV) amplicon
vectors, and in particular, HSV-1 amplicon vectors, which have been
genetically modified and used alone or with consequent genetically
modified HSV virus, to target a selected cell type, such as neoplastic
cells. The present invention also relates to methods of using such
vectors to target a cell, in order to treat a pathol. condition, such as
cancer.

L2 ANSWER 16 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 7

ACCESSION NUMBER: 2000:385448 BIOSIS
DOCUMENT NUMBER: PREV200000385448
TITLE: Cytotoxicity, apoptosis, and viral replication in tumor
cells treated with oncolytic ribonucleotide
reductase-defective herpes simplex type 1 virus (hrR3)
combined with ionizing radiation.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Sun, Fang;
Eling, David J.; Gilpin, Elizabeth; Kipps, Thomas J.;
Chiocca, E. Antonio; Bouvet, Michael
CORPORATE SOURCE: Department of Radiation Oncology, University of California
San Diego Medical Center, 200 West Arbor Drive, MC 8757,
San Diego, CA, 92103-8757, USA
SOURCE: Cancer Gene Therapy, (July, 2000) Vol. 7, No. 7, pp.
1051-1059. print.
ISSN: 0929-1903.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Sep 2000
Last Updated on STN: 8 Jan 2002

AB The viral ribonucleotide reductase (rR)-defective herpes simplex type-1 (HSV-1) virus (hrR3) has been shown previously to preferentially replicate in and kill tumor cells. This selectivity is associated with tumor cell up-regulation of mammalian rR. Ionizing radiation (IR) is currently used in the therapy of many malignancies, including glioblastoma, cervical carcinoma, and pancreatic carcinoma. IR has been shown to up-regulate mammalian rR in tumor cells and appears to increase the efficacy of at least one non-rR-deleted HSV-1 strain in an in vivo tumor model. Here, we test the hypothesis that a single therapeutic radiation fraction will increase the replication and toxicity of hrR3 for malignant cell lines in vitro. PANC-1 pancreatic carcinoma, U-87 glioblastoma, and CaSki cervical carcinoma cell lines were treated with varying doses of IR and subsequently infected with hrR3 or KOS (wild-type HSV-1 strain). Cell survival was then measured using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay and trypan blue exclusion cytometry. At 72 hours posttreatment, irradiation with 2 Gy reduced survival from 100% to 76% in noninfected cells, from 61% to 48% in KOS-infected cells, and from 39% to 27% in hrR3-infected PANC-1 cells. As such, analysis of variance indicated that the toxicity of the two modalities was additive. Similar additivity was seen in U-87 MG and CaSki cells. Absolute survival of hrR3-infected or KOS-infected PANC-1 cells decreased as a function of time after treatment (24-72 hours) and multiplicity of infection (MOI) (0.05-5.0). However, the relative decrease in survival with the addition of IR to hrR3 or KOS in PANC-1 cells was not markedly affected by altering MOI (0.05-5.0), time (24-72 hours), radiation dose (2-20 Gy), or cell culture conditions (confluent/growth arrested). We used fluorescence-activated cell sorter analysis with the cationic lipophilic dye DiOC₆ to quantify a reduction in mitochondrial membrane potential that is associated with apoptosis. Fluorescence-activated cell sorter analysis indicated increased apoptosis in both hrR3- and IR-treated cells at 48-72 hours, with hrR3 alone producing the most induction. Viral yields from PANC-1 cells after irradiation and infection were examined. No significant differences were seen between irradiated and nonirradiated cells in viral replication, with hrR3 producing single-step titers of $3.1 \pm 0.9 \times 10^5$ and $4.0 \pm 1.2 \times 10^5$ plaque-forming units/mL in nonirradiated and irradiated cells. Thus, complementary toxicity was seen between IR and hrR3 or KOS, regardless of cell type, time, MOI, IR dose, or culture conditions, without evidence of augmented apoptosis or viral replication.

L2 ANSWER 17 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:246712 BIOSIS
DOCUMENT NUMBER: PREV200000246712
TITLE: Efficient DNA subcloning through selective restriction endonuclease digestion.
AUTHOR(S): Spear, Matthew A. [Reprint author]
CORPORATE SOURCE: Radiation Oncology, UCSD Medical Center, 200 W. Arbor Dr., San Diego, CA, 92103, USA
SOURCE: Biotechniques, (April, 2000) Vol. 28, No. 4, pp. 660-668. print.
CODEN: BTNQDO. ISSN: 0736-6205.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

AB Described here is a selective restriction endonuclease digestion method that eliminates the electrophoresis step that is usually used during the subcloning of new DNA sequences into typical E. coli-based plasmids. The method increases yield while decreasing laboratory resource and time

utilization. By using donor and acceptor sequences that contain unique restriction sites found only outside of the intended recombination sequences, the initial digestion products can be directly combined without electrophoresis if the ligation step is followed by a selective digestion using the unique restriction enzymes before transformation. This system is based on the several order of magnitude decrease in transformation efficiency of linearized compared to a circular plasmids. As an example, this method was used to obtain recombinants between a 3.6 kb acceptor plasmid and 3.0 kb insert following one ligation reaction after the failure of nine standard reactions using similar amounts of input DNA. It is particularly applicable to situations in which low subcloning efficiencies are expected. The technique can be extended to a large percentage of planned recombinations by using non-identical compatible cohesive or blunt-ended fragments, or site-directed mutagenesis.

L2 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:261585 CAPLUS
DOCUMENT NUMBER: 133:172714
TITLE: Efficient DNA subcloning through selective restriction endonuclease digestion
AUTHOR(S): Spear, Matthew A.
CORPORATE SOURCE: University of California at San Diego, San Diego, CA, 92103, USA
SOURCE: BioTechniques (2000), 28(4), 660,662,664,666,668
CODEN: BTNQDO; ISSN: 0736-6205
PUBLISHER: Eaton Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Described here is a selective restriction endonuclease digestion method that eliminates the electrophoresis step that is usually used during the subcloning of new DNA sequences into typical E. coli-based plasmids. The method increases yield while decreasing laboratory resource and time utilization. By using donor and acceptor sequences that contain unique restriction sites found only outside of the intended recombination sequences, the initial digestion products can be directly combined without electrophoresis if the ligation step is followed by a selective digestion using the unique restriction enzymes before transformation. This system is based on the several order of magnitude decrease in transformation efficiency of linearized compared to circular plasmids. As an example, this method was used to obtain recombinants between a 3.6 kb acceptor plasmid and 3.0 kb insert following one ligation reaction after the failure of nine standard reactions using similar amounts of input DNA. It is particularly applicable to situations in which low subcloning efficiencies are expected. The technique can be extended to a large percentage of planned recombinations by using non-identical compatible cohesive or blunt-ended fragments, or site-directed mutagenesis.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:224982 BIOSIS
DOCUMENT NUMBER: PREV200000224982
TITLE: Phage display epitopes selected against viable glioblastoma cells for insertion into an HSV-1 amplicon vector targeting system.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Ladner, Robert; Schuback, Deborah E.; Brandt, Curtis R.; Sun, Fang; Beltzer, James; Breakefield, Xandra O.
CORPORATE SOURCE: Dept of Neurology, MA Gen Hosp, Boston, MA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 466. print.
Meeting Info.: 91st Annual Meeting of the American

Association for Cancer Research. San Francisco, California,
USA. April 01-05, 2000.
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 May 2000
Last Updated on STN: 5 Jan 2002

L2 ANSWER 20 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 8

ACCESSION NUMBER: 2000:179851 BIOSIS
DOCUMENT NUMBER: PREV200000179851
TITLE: Improved method for transport of living cell cultures.
AUTHOR(S): Rainov, Nikolai G. [Reprint author]; Truempler, Christel;
Quinones, Ariel; Spear, Matthew A.; Kramm, Christof M.
CORPORATE SOURCE: Department of Neurosurgery, Laboratory of Molecular
Oncology, Martin-Luther-University Halle-Wittenberg, Halle,
Germany
SOURCE: Biotechnology Letters, (March, 2000) Vol. 22, No. 5, pp.
383-385. print.
CODEN: BILED3. ISSN: 0141-5492.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 May 2000
Last Updated on STN: 4 Jan 2002

AB An easy and cost-effective method for transport of living cell cultures
which avoids the use of dry ice and prevents bacterial contamination is
described. Cells are suspended in buffered culture medium in sealed and
insulated 2 ml cryovials and are able to grow and survive in substantial
numbers during several days of storage and shipment at ambient
temperature. Replating results in an identical repopulation in all cell
lines. Not only tumor cells but also fibroblasts seem to tolerate well
this improved method for shipment.

L2 ANSWER 21 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 2000:245019 BIOSIS
DOCUMENT NUMBER: PREV200000245019
TITLE: Mechanisms of radiation sensitization by recombinant
methioninase (rMETase).
AUTHOR(S): Sun, Fang [Reprint author]; Tan, Yuying; Xu, Mingxu; Miki,
Kenji; Bouvet, Michael; Hoffman, Robert M.; Spear,
Matthew A.
CORPORATE SOURCE: AntiCancer Inc, San Diego, CA, USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (March, 2000) No. 41, pp. 293. print.
Meeting Info.: 91st Annual Meeting of the American
Association for Cancer Research. San Francisco, California,
USA. April 01-05, 2000.
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

L2 ANSWER 22 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 2000:90707 BIOSIS
DOCUMENT NUMBER: PREV200000090707
TITLE: Tolerance of autologous and allogeneic bone grafts to

AUTHOR(S): Spear, Matthew A. [Reprint author]; Dupuy, Damian E.; Park, Jenine J.; Halpern, Elkan F.; Spiro, Ira J.

CORPORATE SOURCE: Radiation Oncology, University of California at San Diego, 200 W. Arbor Drive, San Diego, CA, 92103-8757, USA

SOURCE: International Journal of Radiation Oncology Biology Physics, (Dec. 1, 1999) Vol. 45, No. 5, pp. 1275-1280. print.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Mar 2000
Last Updated on STN: 3 Jan 2002

AB Purpose: To examine the effect of perioperative irradiation on bone graft healing and functional integrity. Methods and Materials: Fifty-five bone grafts (10 autologous and 45 allogeneic) performed between 1978 and 1995 were evaluated retrospectively. Sixteen received preoperative radiation, 11 received postoperative, and 13 were treated with a combination of pre- and postoperative radiation. Fifteen nonirradiated grafts were randomly selected to serve as controls. Twenty-three of the grafts were placed in patients who received chemotherapy in the perioperative period. Functional graft survival and radiographic healing quality were evaluated. Results: Overall rates of graft survival at 1 year were 89% for autografts and 79% for allografts. Graft survival rates were 86% and 68% at 1 and 5 years for the irradiated group, and 67% and 58% for the control group. No significant difference was seen in the Kaplan-Meier graft survival curves of the two groups. There was a nonsignificant trend toward improved radiographic healing quality in the control group. No significant differences in outcome based on treatment chronology were found with survival rates of 88% for preoperative treatment and 100% for postoperative treatment. No relation between outcome and bone dose (preoperative + postoperative dose), graft dose (postoperative dose), or mean dose/day was found. There was a trend ($p = 0.0525$) toward worse outcome seen in the Kaplan-Meier curves of patients who received chemotherapy. This difference, however, was not seen in the 1-year survival rates or healing quality. Tobacco use tended toward predicting failure, with 63% graft survival compared to 85% in nonsmokers ($p = 0.09$). Healing quality was significantly lower in the smoking group. Conclusion: The low failure rate of grafts in irradiated sites, overall and compared to controls from this study and relevant literature, as well as the lack of dose and time effects, does not support significant deviation from the indicated treatment regimen for patients who have received or are expected to receive a graft. The trend toward decreased quality of radiographic bone healing, and data published in relevant literature indicating improved healing when radiation is withheld until 3-4 weeks postoperatively suggest this delay should be attempted when not expected to otherwise compromise patient outcome. A nonsignificant trend only for the effect of chemotherapy on bone grafts was seen, thus we do not recommend changes in its use as appropriate for disease management other than a preference against use during the immediate perioperative period.

L2 ANSWER 23 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 9

ACCESSION NUMBER: 1999:47482 BIOSIS

DOCUMENT NUMBER: PREV199900047482

TITLE: Gene therapy of gliomas: Receptor and transcriptional targeting.

AUTHOR(S): Spear, Matthew A. [Reprint author]

CORPORATE SOURCE: UCSD Med. Cent., Radiation Oncol., 200 W. Arbor Dr., No. 8757, San Diego, CA 92103, USA

SOURCE: Anticancer Research, (Sept.-Oct., 1998) Vol. 18, No. 5A, pp. 3223-3231. print.

CODEN: ANTRD4. ISSN: 0250-7005.

DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Feb 1999
Last Updated on STN: 10 Feb 1999
AB Through incremental increases in the overall therapeutic ratio of combined modality regimens, each addition of unique selective toxicity to a tumor moves one step closer to a cure. The primary advantage of adding gene therapy strategies to current oncologic regimens is the ability to design multiple levels of unique biologic selectivity into vectors using recombinant technology. This article presents an overview of current and potential methods for designing vectors targeted to high grade gliomas through selective cell entry or transcriptional regulation. Cell entry based methodologies are founded on increasing relative uptake of the vector through the chemical or recombinant addition of epitopes which bind to receptors selectively expressed on target cells. Transcriptional targeting utilizes promoter and enhancer systems which have potential for selectively activating transcription for transgene expression or vector propagation in target cells.

L2 ANSWER 24 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 10

ACCESSION NUMBER: 1998:391606 BIOSIS
DOCUMENT NUMBER: PREV199800391606
TITLE: Mapping the in vivo distribution of herpes simplex virions.
AUTHOR(S): Schellingerhout, Dawid; Bogdanov, Alexei, Jr.; Marecos, Edgardo; Spear, Matthew; Breakefield, Xandra; Weissleder, Ralph [Reprint author]
CORPORATE SOURCE: Mass. General Hosp., 149 13th St., Room 5403, Charlestown, MA 02129, USA
SOURCE: Human Gene Therapy, (July 20, 1998) Vol. 9, No. 11, pp. 1543-1549. print.
ISSN: 1043-0342.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 1998
Last Updated on STN: 10 Sep 1998

AB We describe a method for labeling enveloped viral particles with a radiotracer, indium-111, allowing labeled viruses to be traced in vivo by nuclear imaging. After initial optimization experiments, a labeling efficiency of 83% (incorporation yield) was achieved for herpes simplex virus (HSV), resulting in a specific activity of 30. μ Ci/10⁹ PFU. The labeling procedure did not significantly reduce the infectivity of the labeled virus and the virus did not release any significant amounts of the radionuclide within 12 hr after labeling. Sequential imaging of animals after intravenous administration of the labeled virus showed fast accumulation in the liver and redistribution from the blood pool (immediately after injection) to liver and spleen (12-24 hr after injection). At 12 hr after injection 7% of the virus-associated ¹¹¹In had been eliminated from the body and the remaining organ distribution of the virus was as follows: spleen 28.7 +- 5.4% ID/g; liver, 26.0 +- 5.1% ID/g; kidney, 9.8 +- 3.1% ID/g; lung, 5.7 +- 1.0% ID/g; and lower amounts in other organs. Our results indicate that the described method allows qualitative and quantitative assessment of viral biodistribution in vivo by nuclear imaging.

L2 ANSWER 25 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN

ACCESSION NUMBER: 1998:168840 BIOSIS
DOCUMENT NUMBER: PREV199800168840
TITLE: Individualizing management of aggressive fibromatoses.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Jennings, L. Candace; Mankin, Henry J.; Spiro, Ira J.; Springfield,

CORPORATE SOURCE: Dempsy S.; Gebhardt, Mark C.; Rosenberg, Andrew E.; Efird, James T.; Suit, Herman D.
Dep. Radiation Oncol., Massachusetts Gen. Hosp., Boston, MA 02114, USA

SOURCE: International Journal of Radiation Oncology Biology Physics, (Feb. 1, 1998) Vol. 40, No. 3, pp. 637-645. print.
CODEN: IOBPD3. ISSN: 0360-3016.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Apr 1998
Last Updated on STN: 6 Apr 1998

AB Purpose: To examine prognostic indicators in aggressive fibromatoses that may be used to optimize case-specific management strategy. Methods and Materials: One hundred and seven fibromatoses presenting between 1971 and 1992 were analyzed. The following treatment modalities were utilized: (a) surgery alone for 51 tumors; (b) radiation alone for 15 tumors; and (c) radiation and surgery (combined modality) for 41 tumors. Outcome analysis was based on 5-year actuarial local control rates. Results: Control rates among surgery, radiation therapy, and combined modality groups were 69%, 93%, and 72%. Multivariate analysis identified age <18 years, recurrent disease, positive surgical margins, and treatment with surgery alone as predictors for failure. Patients treated with surgery alone had control rates of 50% (3 of 6) for gross residual, 56% for microscopically positive margins, and 77% for negative margins. Radiation and surgery resulted in rates of 59% for gross residual, 78% for microscopically positive margins, and 100% (6 of 6) for negative margins. For recurrent vs. primary tumors, control was achieved in 48% vs. 77%, 90% vs. 100% (5 of 5), and 67% vs. 79% in the Surgery, Radiation, and Combined modality Groups, respectively. Patients presenting with multiple disease sites tended to have aggressive disease. A radiation dose-control relation to > 60 Gy was seen in patients with unresected or gross residual disease. Of the patients, 23 with disease involving the plantar region had a control rate of 62%, with significantly worse outcomes in children. Conclusions: These results are consistent with those found in the relevant literature. They support primary resection with negative margins when feasible. Radiation is a highly effective alternative in situations where surgery would result in major functional or cosmetic defects. When negative surgical margins are not achieved in recurrent tumors, radiation is recommended. Perioperative radiation should be considered in other high-risk groups (recurrent disease, positive margins, and plantar tumors in young patients). Doses of 60-65 Gy for gross disease and 50-60 Gy for microscopic residual are recommended. Observation may be considered for primary tumors with disease remaining in situ when they are located such that progression would not cause significant morbidity. Although plantar lesions in children may represent a group at high risk for recurrence or aggressive behavior, the greater potential for radiation-induced morbidity in this group must also temper its use. Given the inconsistent nature and treatment response of this tumor, it is fundamental that treatment recommendations should be made based on the risk:benefit analysis for the individual patient, dependent on tumor characteristics and location, as well as patient characteristics and preferences.

L2 ANSWER 26 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 11

ACCESSION NUMBER: 1998:230569 BIOSIS
DOCUMENT NUMBER: PREV199800230569
TITLE: Targeting gene therapy vectors to CNS malignancies.
AUTHOR(S): Spear, Matthew A. [Reprint author]; Herrlinger,
Ulrich; Rainov, Nikolai; Pechan, Peter; Weissleder, Ralph;
Breakefield, Xandra O.
CORPORATE SOURCE: Dep. Neurol., Mol. Neurogenet. Unit, Mass. Gen. Hosp.,
Bldg. 149, 13th St., Charlestown, MA 02129, USA
SOURCE: Journal of Neurovirology, (April, 1998) Vol. 4, No. 2, pp.

133-147. print.
ISSN: 1355-0284..
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 May 1998
Last Updated on STN: 20 May 1998
AB Gene therapy offers significant advantages to the field of oncology with the addition of specifically and uniquely engineered mechanisms of halting malignant proliferation through cytotoxicity or reproductive arrest. To confer a true benefit to the therapeutic ratio (the relative toxicity to tumor compared to normal tissue) a vector or the transgene it carries must selectively affect or access tumor cells. Beyond the selective toxicities of many transgene products, which frequently parallel that of contemporary chemotherapeutic agents, lies the potential utility of targeting the vector. This review presents an over-view of current and potential methods for designing vectors targeted to CNS malignancies through selective delivery, cell entry, transport or transcriptional regulation. The topic of delivery encompasses physical and pharmaceutical means of increasing the relative exposure of tumors to vector. Cell entry based methodologies are founded on increasing relative uptake of vector through the chemical or recombinant addition of ligand and antibody domains which selectively bind receptors expressed on target cells. Targeted transport involves the potential for using cells to selectively carry vectors or transgenes into tumors. Finally, promoter and enhancer systems are discussed which have potential for selectivity activating transcription to produce targeted transgene expression or vector propagation.

L2 ANSWER 27 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:56529 BIOSIS
DOCUMENT NUMBER: PREV199800056529
TITLE: Benign and low-grade tumors of the soft tissues: Role for radiation therapy.
AUTHOR(S): Suit, Herman D. [Reprint author]; Spiro, Ira J.; Spear, Matthew
CORPORATE SOURCE: Dep. Radiol. Med., Mass. Gen. Hosp., Harvard Med. Sch., Boston, MA 02114, USA
SOURCE: Verweij, J. [Editor]; Pinedo, H. M. [Editor]; Suit, H. D. [Editor]. Cancer Treatment and Research, (1997) pp. 95-105. Cancer Treatment and Research; Soft tissue sarcomas: Present achievements and future prospects. print.
Publisher: Kluwer Academic Publishers, 101 Phillip Drive, Norwell, Massachusetts 02061, USA; Kluwer Academic Publishers, PO Box 989, 3300 AZ Dordrecht, Netherlands.
Series: Cancer Treatment and Research.
ISSN: 0927-3042. ISBN: 0-7923-9913-7.

DOCUMENT TYPE: Book
Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998

L2 ANSWER 28 OF 28 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 12

ACCESSION NUMBER: 1993:209673 BIOSIS
DOCUMENT NUMBER: PREV199395110898
TITLE: Toxicology of daily administration to mice of the radiation potentiator SR-4233 (WIN-59075).
AUTHOR(S): Spiegel, James F.; Spear, Matt A.; Brown, J. Martin [Reprint author]
CORPORATE SOURCE: Dep. Radiation Oncol., Stanford Med. Cent., CBRL, Stanford, CA 94305-5468, USA

SOURCE: Radiotherapy and Oncology, (1993) Vol. 26, No. 1, pp.
79-81.

CODEN: RAONDT. ISSN: 0167-8140.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 23 Apr 1993

Last Updated on STN: 9 Jun 1993

AB We have investigated the feasibility of administration of an effective dose of the hypoxic cytotoxin, SR 4233, Monday-Friday daily for 6 weeks. From a thorough hematological, histopathological and clinical chemistry evaluation throughout the course and during a 3-week recovery period, we conclude that daily administration of a radiopotentiating dose of SR 4233 in mice is well tolerated and that bone marrow suppression is likely to be the dose-limiting toxicity.

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E SPEAR MATTHE?/AU

| | |
|----|---------------------------------------|
| L1 | 44 E2-E6 |
| L2 | 28 DUP REM L1 (16 DUPLICATES REMOVED) |
| L3 | 12 CELLS AND L2 |
| L4 | 4 LIBRARY AND L2 |
| L5 | 3 LIGAND AND L2 |
| L6 | 1 APOPTOSIS AND L2 |

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=> logoff hold

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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NEWS 3 JUL 02 SCISEARCH enhanced with complete author names
NEWS 4 JUL 02 CHEMCATS accession numbers revised
NEWS 5 JUL 02 CA/CAplus enhanced with utility model patents from China
NEWS 6 JUL 16 CAplus enhanced with French and German abstracts
NEWS 7 JUL 18 CA/CAplus patent coverage enhanced
NEWS 8 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9 JUL 30 USGENE now available on STN
NEWS 10 AUG 06 CAS REGISTRY enhanced with new experimental property tags
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NEWS 23 SEP 24 EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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